

FIG. I

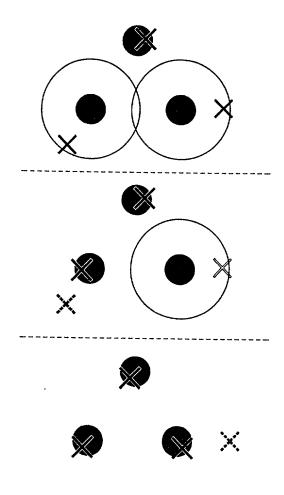
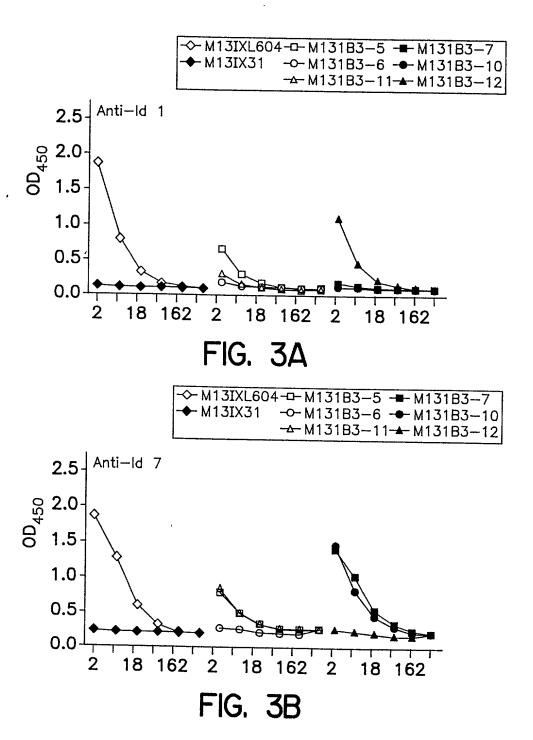


FIG. 2



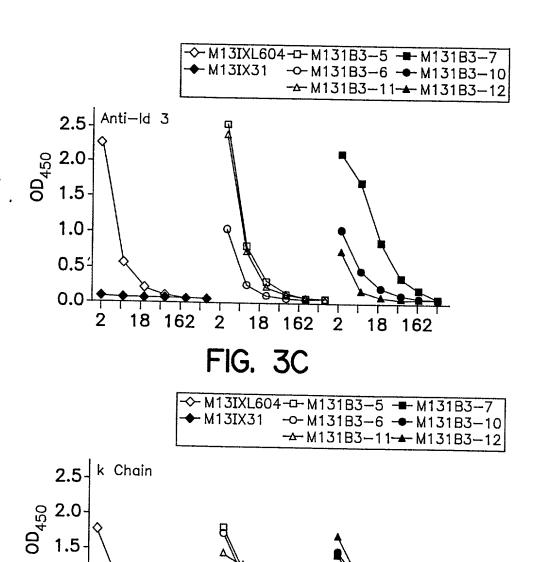


FIG. 3D

18 162

2

18 162

2

1.0

0.5

0.0

2

18 162

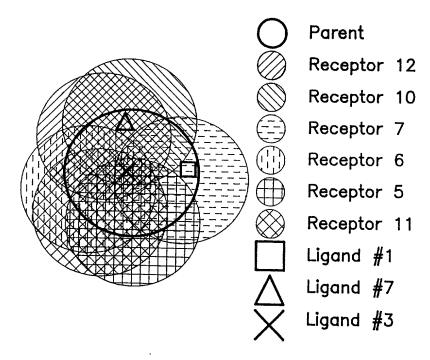
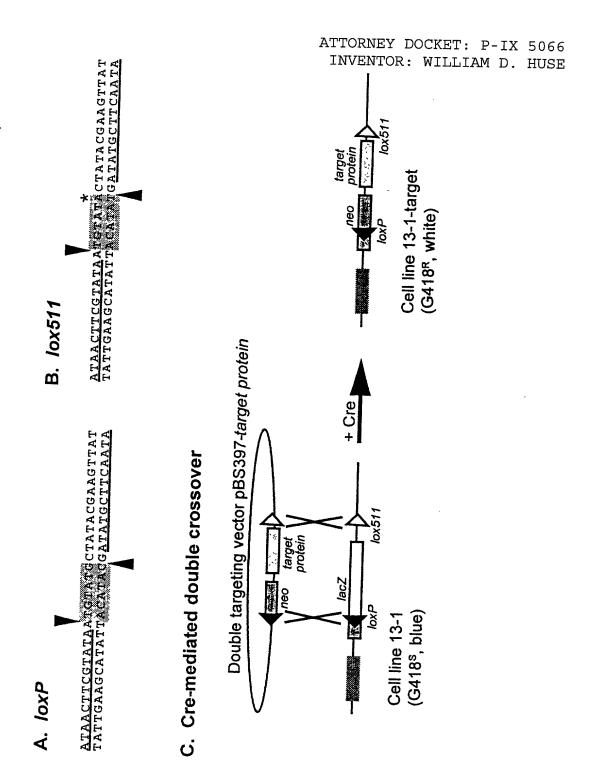


FIG. 4



SEVVSTNFRDASGPAM<u>TEIGEÖPWG-REFA</u>LRDPAGNCVHFVAEEQD----KPL----GILHPNTSLKDQWWDERDFAVIDPDNNLISFFQQIKS----KSV-GIQETSSGYPRIHAPELOEWGGTMAALVDPDGTLLRLIQNELLAGIS 80 MAKLTSAVDVLTARDVAGAVEEWTDRIGESR<u>DFVEDDFA</u>GVVRDD -MRMLQSI PALPVGDIKKSIGEYCDKIGETLVHHEDGFAVLMCNE --MTDQATPNIPSRDFDSTAARY-ERIGEGIVFRDAGWMILQRGD 10 20 30 40 \*\*\* \*\* VTLFISAVODO ---\* \* \* Sh ble Sa ble Tn5 ble Sh ble Sa ble Sh ble Sa ble Tn5 ble In5 ble

## Cre recombinase-mediated targeted integration of BRP variants in 13-1 mammalian cells

400 μg/ml geneticin

Selection of site-specific integrants



## Zeocin ( $\mu g/ml$ ) $\rightarrow$

500	1000	2500	5000	Comments	
+	+	+	+	Beneficial mutation	
+	+	+	_	Wild-type	
+	+	T	<b>-</b>	Detrimental mutation	
+			T -	Detrimental mutation	
T -	Τ –	_	T -	Non-functional BRP	

<b>1</b>	O VCKVDCMNII 1	<b>20</b> CVFGGTVTAF	30	40	KDOSI TK
60	7	0	80	90	100
		DQSFPGFHGS			
110 KPKNATVLIV	<b>120</b> Wiygggfqt(	130 STSSLHVYDG	] KFLARVER	140 VIVVSMNY	150 RVGALGF
		- <b>180</b> Qlalqwvqkn			
SLHLLSPGSI	770 HSLFTRAIL(	<b>230</b> QSGSFNAPWA	VTSLYEAR VTSLYEAR	J NRTLNLAK	200 LTGCSRE
260	270		290	_	300
NETELIKCL	RNKDPQEIL	LNE <u>AFVVPYG</u>	TPLSVNFG	PTVDGDFL	TDMPDIL
310 LELGQFKKT(	<b>320</b> Qilvgvnkde	<b>330</b> EG <u>taflvy</u> ga	<b>340</b> PGFSKDNN	350 SIITRKEF	) QEGLKIF
<b>360</b> FPGVSEFGKI	<b>370</b> ESILFHYTDV	<b>380</b> VVDDQRPENY	390 Realgdvv	400 GDYNFICP	ALEFTKK
410	420				D D
FSEWGNNAF1	EYYEEHRSSE	KL <u>PWPEWMGV</u>			RDNYTKA
160 EEILSRSIVI	<mark>470</mark> KRWANFAKY(	<b>480</b> GNPNETQNNS	490 TSWPVFKS	500 TEOKYLTL	510 NTESTRI
MTKLRAQQC:	AU RFWTSFFPK'	<b>530</b> Vlemtgnide	J4U CAEWEWKAG	FHRWNNYM	MDWKNQF
570	1	-			
NDYTSKKES					